

WHAT IS CLAIMED IS:

1. A method for identifying a compound that binds to a target RNA,  
said method comprising
  - 5 (a) contacting a detectably labeled target RNA molecule with a  
library of compounds under conditions that permit direct  
binding of the labeled target RNA to a member of the library  
of compounds and the formation of a detectably labeled target  
RNA:compound complex, wherein the target RNA is a region  
of 28S rRNA or contains a premature stop codon; and
  - 10 (b) detecting the formation of a detectably labeled target  
RNA:compound complex.
2. A method for identifying a compound to test for its ability to  
modulate premature translation termination or nonsense-mediated mRNA decay, said  
method comprising:
  - 15 (a) contacting a detectably labeled target RNA molecule with a  
library of compounds under conditions that permit direct  
binding of the labeled target RNA to a member of the library  
of compounds and the formation of a detectably labeled target  
RNA:compound complex, wherein the target RNA is a region
  - 20 (b) detecting a detectably labeled target RNA:compound complex  
formed in step(a), so that if a target RNA:compound complex  
is detected then the compound identified is tested for its  
ability to modulate premature translation or nonsense-  
mediated mRNA delay.
- 25 3. A method for identifying a compound that binds to a target RNA,  
said method comprising detecting the formation of a detectably labeled target  
RNA:compound complex formed from contacting a detectably labeled RNA with a member  
of a library of compounds under conditions that permit direct binding of the labeled target  
30 RNA to a member of the library of compounds and the formation of a detectably labeled  
target RNA:compound complex, wherein the target RNA is a region of 28S rRNA or  
contains a premature stop codon.

4. A method of identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

- 5 (a) contacting a detectably labeled target RNA molecule with a library of compounds under conditions that permit direct binding of the labeled target RNA to a member of the library of compounds and the formation of a detectably labeled target RNA:compound complex, wherein the target RNA is a region of 28S rRNA or contains a premature stop codon; and
- 10 (b) detecting a detectably labeled target RNA:compound complex formed in step(a), so that if a target RNA:compound complex is detected, then
- 15 (c) contacting the compound with a cell-free translation mixture and a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene, wherein the reporter gene contains a premature stop codon; and
- 20 (d) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a negative control.

5. A method of identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

- 25 (a) contacting a detectably labeled target RNA molecule with a library of compounds under conditions that permit direct binding of the labeled target RNA to a member of the library of compounds and the formation of a detectably labeled target RNA:compound complex, wherein the target RNA is a region of 28S rRNA or contains a premature stop codon; and
- 30 (b) detecting a detectably labeled target RNA:compound complex formed in step(a), so that if a target RNA:compound complex is detected, then

- (c) contacting the compound with a cell containing a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene, wherein the reporter gene contains a premature stop codon; and
- 5 (d) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a
- 10 negative control.

6. The method of claim 1, 2, 3, 4 or 5, wherein each compound in the library is attached to a solid support.

7. The method of claim 6, wherein the solid support is a silica gel, a resin, a derivatized plastic film, a glass bead, cotton, a plastic bead, a polystyrene bead, an

15 aluminum gel, a glass slide or a polysaccharide.

8. The method of claim 1, 2, 3, 4 or 5, wherein the library of compounds is attached to a chip.

9. The method of claim 1, 2, 3, 4 or 5, wherein the detectably labeled

20 RNA is labeled with a fluorescent dye, phosphorescent dye, ultraviolet dye, infrared dye, visible dye, radiolabel, enzyme, spectroscopic colorimetric label, affinity tag, or nanoparticle.

10. The method of claim 1, 2, 3, 4 or 5, wherein the compound is a combinatorial library of compounds comprising peptoids; random biooligomers;

25 diversomers such as hydantoins, benzodiazepines and dipeptides; vinylogous polypeptides; nonpeptidal peptidomimetics; oligocarbamates; peptidyl phosphonates; peptide nucleic acid libraries; antibody libraries; carbohydrate libraries; or small organic molecule libraries.

11. The method of claim 10, wherein the small organic molecule libraries are libraries of benzodiazepines, isoprenoids, thiazolidinones, metathiazanones, pyrrolidines, morpholino compounds, or diazepindiones.
- 5 12. The method of claim 1, 2, 3, 4 or 5, wherein the detectably labeled target RNA:compound complex is detected by electrophoresis, fluorescence spectroscopy, surface plasmon resonance, mass spectrometry, scintillation, proximity assay, structure-activity relationships ("SAR") by NMR spectroscopy, size exclusion chromatography, affinity chromatography, or nanoparticle aggregation.
- 10 13. The method of claim 1, 2, 3, 4 or 5, wherein the method further comprises determining the structure of the compound.
14. The method of claim 13, wherein the structure of the compound is determined by mass spectroscopy, NMR, X-ray crystallography, Edman degradation or vibration spectroscopy.
- 15 15. The method of claim 1, 2, 3, 4 or 5, wherein the premature stop codon is UAG, UGA or UAA.